Diseases of the endocrine system 2024
Lecture 1: Pituitary gland

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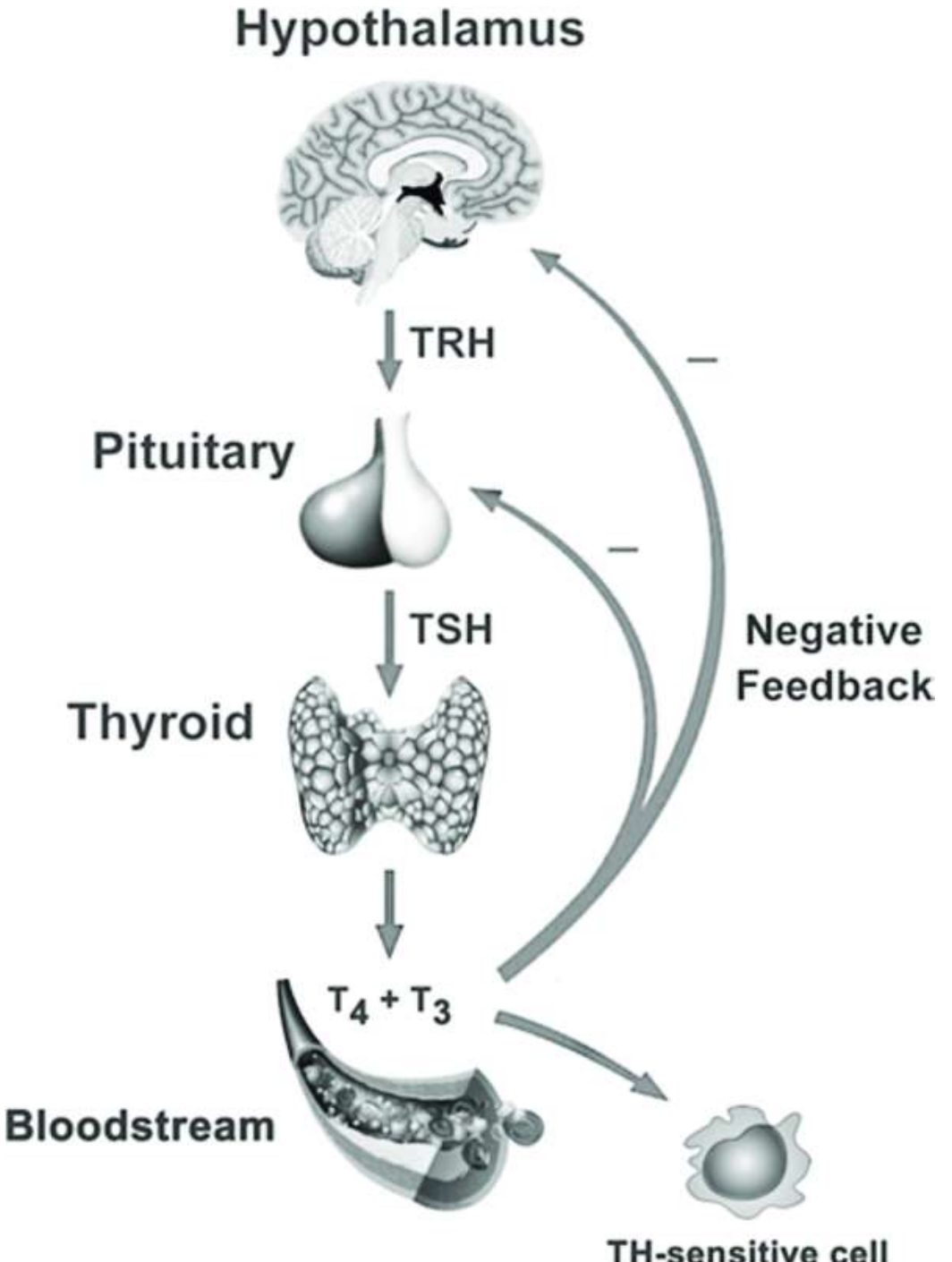
Introduction to the endocrine system

- The endocrine system is composed of glands , distributed on various anatomical locations, that work together to maintain homeostasis (body's metabolic equilibrium).
- Endocrine glands secrete hormones, that circulate in the blood to reach and affect the function of target cells.
- Most hormones are secreted in response to trophic factors that are secreted in response to certain metabolic needs.
- Production of hormones downregulates the activity of the gland that secretes the trophic hormone= negative feedback or feedback inhibition.
- See example on next slide..

Example

- TRH (thyroid releasing hormone) and TSH (thyroid stimulating hormone) are the trophic hormones responsible for stimulation of thyroid hormone production (T3 and T4)
- Once there is enough T3 and T4 ,the TRH and TSH are decreased.
- This maintains the balance of these hormones .



Endocrine system diseases general principles/1

The diseases of the endocrine system can be due to:

1. Mass effect
2. Disordered hormonal production (Under or over production)
3. End organ resistence to the effect of the hormone.

Endocrine system diseases general principles/2

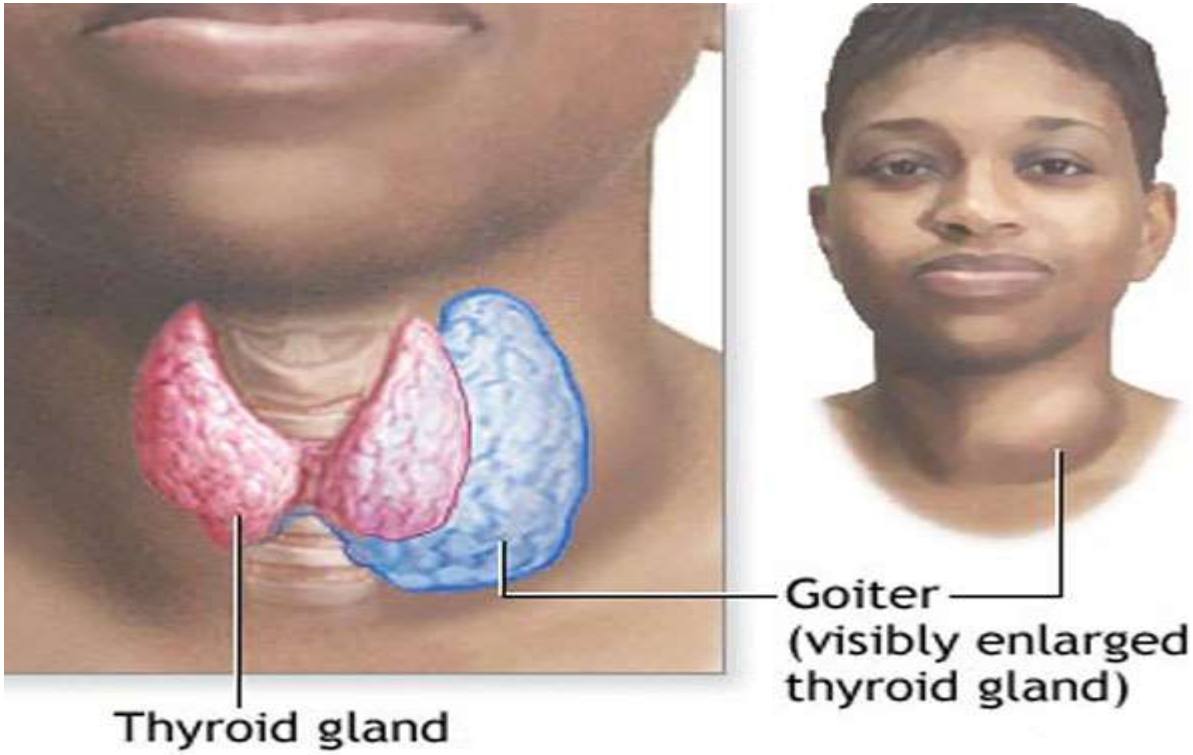
- Mass effect means an enlargement of the gland which can compress adjacent structures.
- Mass effect can be due to neoplastic or non-neoplastic conditions
- Neoplastic include: adenoma and carcinoma
- Non neoplastic= hyperplasia

Endocrine system diseases general principles/3

- The other group of diseases affecting endocrine glands are: abnormal hormonal secretion
- This can be over or under production due to several causes that will be discussed later
- IMPORTANT NOTE: there is no relation between mass effect and hormonal abnormalities.
- Patients might have a mass with normal, low or high hormonal secretion.
- Also hormone overproduction **is not always** associated with a mass

REMEMBER

- A large gland doesn't predict hormonal level !!



Endocrine system diseases general principles/4

- End organ resistance means that the gland is secreting the hormone but the target organ is not responding to it . This occurs in some types of diabetes.

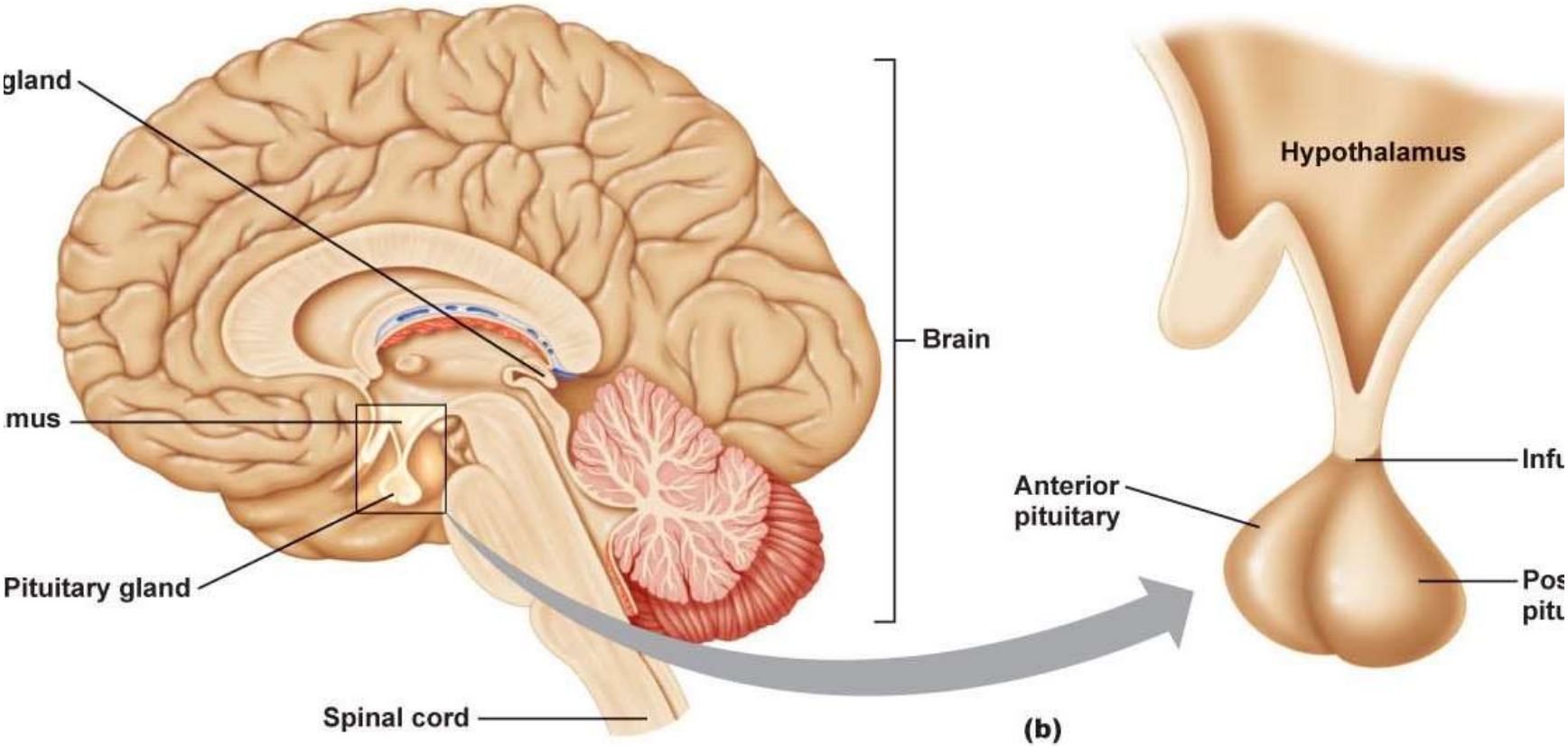
PITUITARY GLAND: THE ORCHISTRA MAESTRO

- The hormones secreted from the pituitary gland control levels of hormones secreted from all other endocrine glands.

Pituitary gland

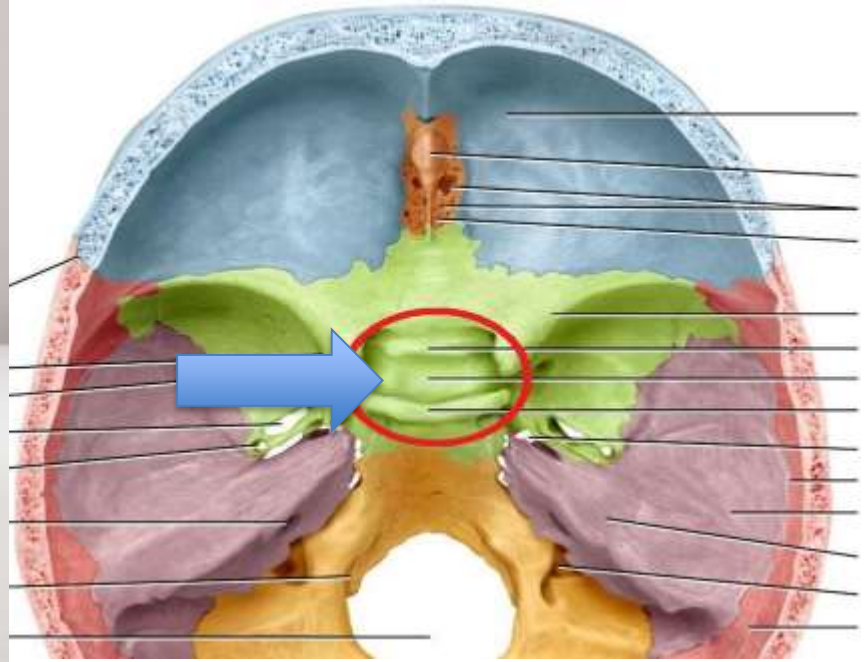
- Small, bean shaped structure that lies at the base of the brain within the sella turcica.

Pituitary gland



اَلسَّرْجُ التُّرْكِيُّ= Sella turcica = pituitary fossa

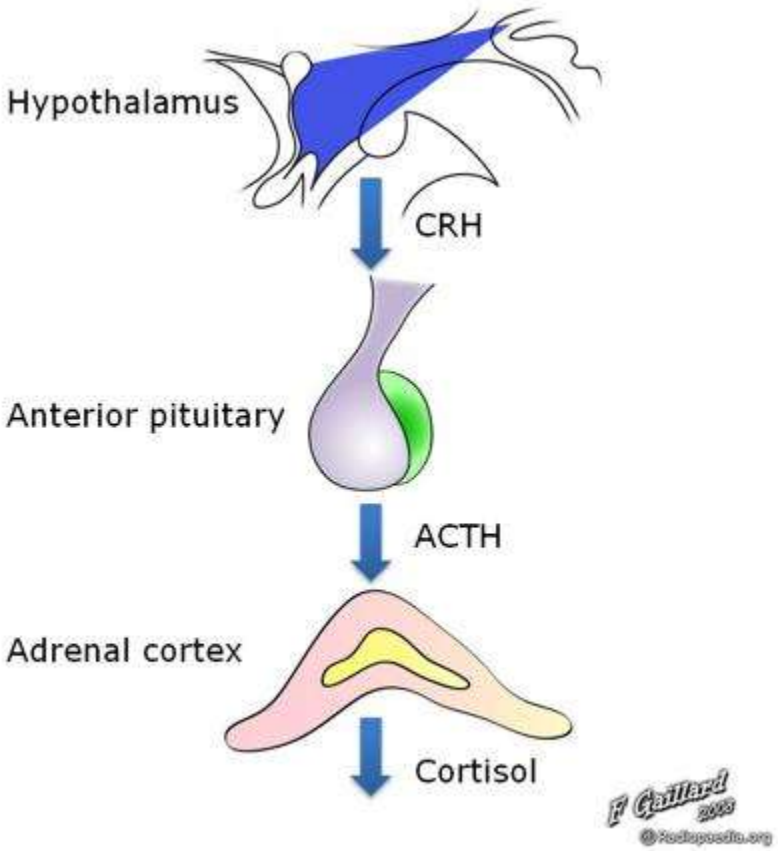
- The **sella turcica** (Latin for Turkish seat) is a saddle-shaped depression in the body of the sphenoid bone of the skull.

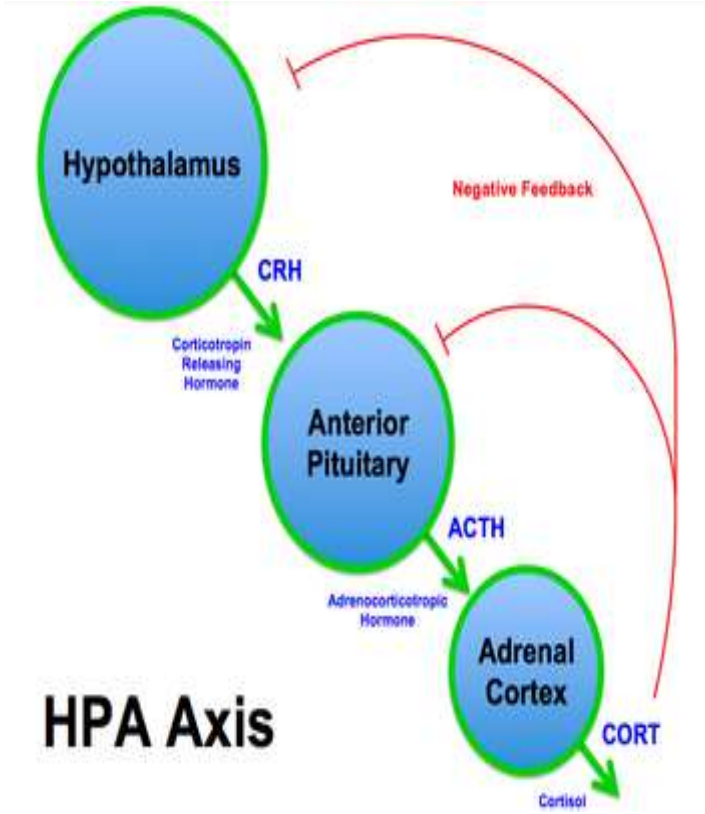


The hypothalamus (تحت المهاد) controls the pituitary (الْغُدَّة النُّخَامِيَّة)

The production of most pituitary hormones is controlled by positively and negatively acting factors from the hypothalamus which are carried to the anterior pituitary by a **portal vascular system.**

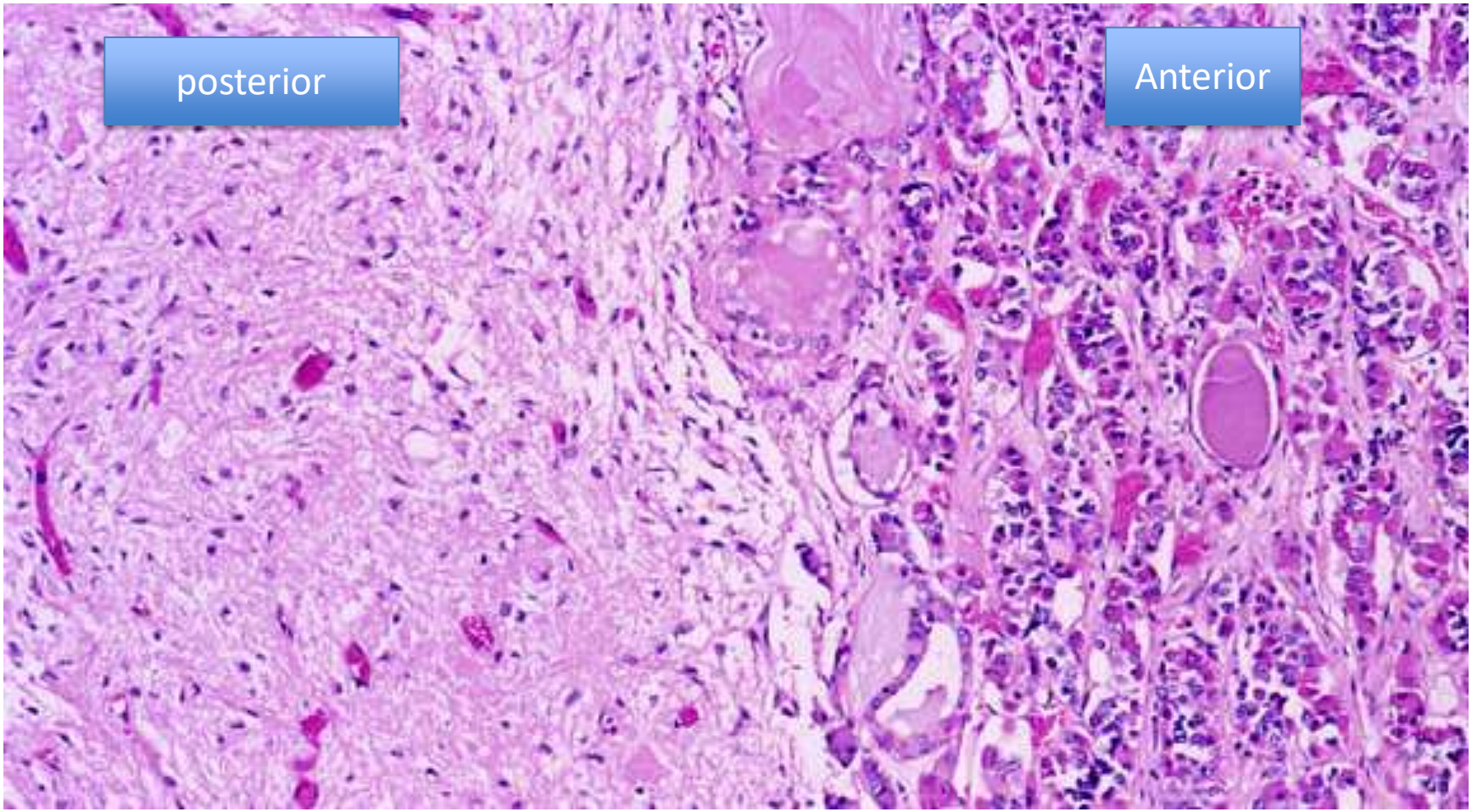
Examples of hypothalamic- pituitary axis.





- The pituitary gland is composed of two morphologically and functionally distinct components: the **anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis)**
- The *anterior pituitary* constitutes about 80% of the gland.

Anterior versus posterior pituitary



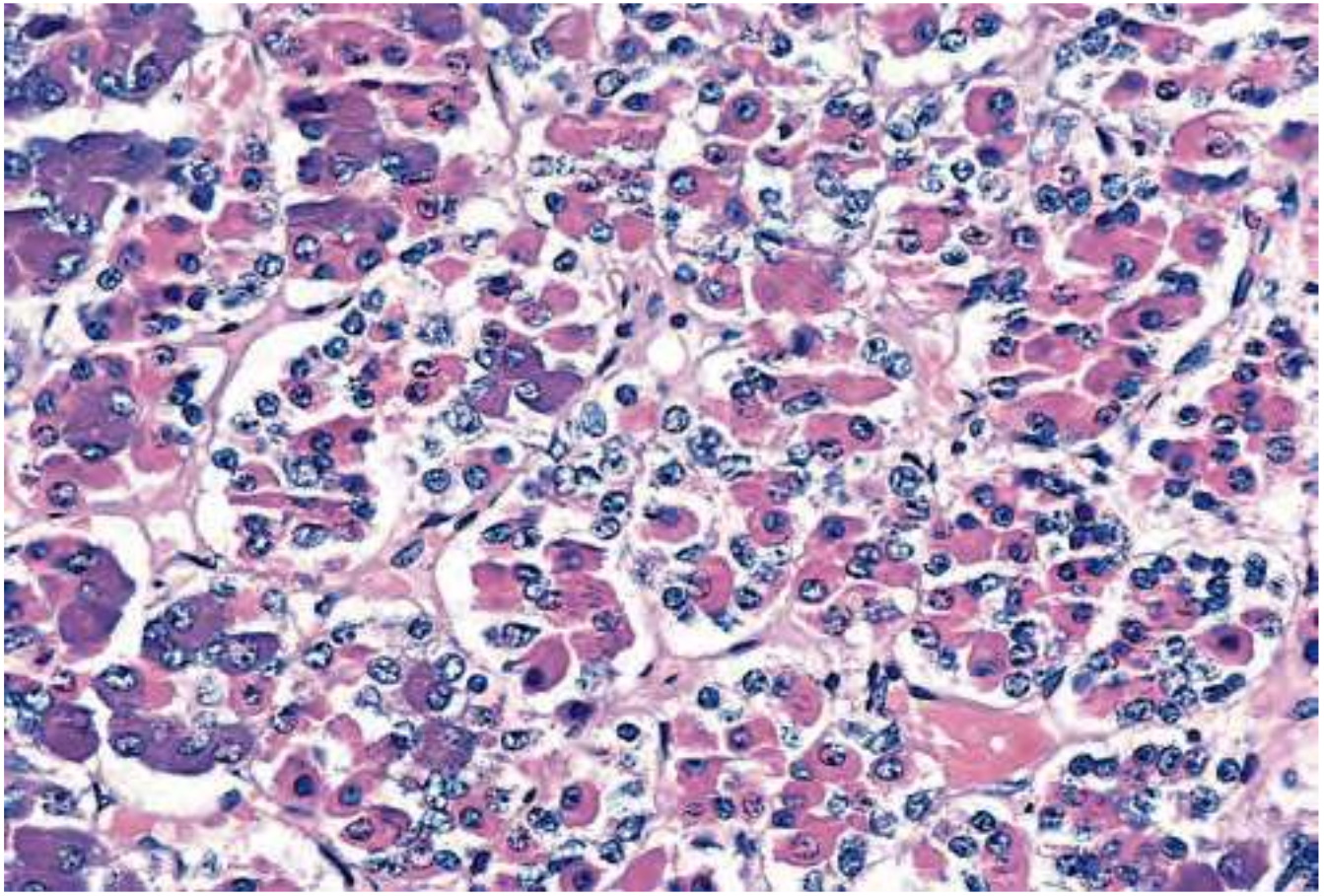
ANTERIOR VERSUS POSTERIOR PITUTARY LOBES

	ANTERIOR PITUITARY	POSTERIOR PITUITARY
histology	Epithelial cells	Glial cells and neuronal axons
Embryological origin	Oral mucosa	Neural crest
Hormones secreted	TSH, PRL, ACTH, GH, FSH , LH.	ADH and oxytocin (*synthesized in hypothalamus but stored in posterior pituitary*)

Anterior pituitary

- The anterior pituitary is composed of epithelial cells that secrete trophic hormones like: TSH, PRL, ACTH..

Anterior pituitary/ epithelial cells



Posterior pituitary

- The *posterior pituitary* consists of **modified glial cells** (*pituicytes*) and axonal processes extending from the hypothalamus through the pituitary stalk to the posterior lobe (*axon terminals*).

- The posterior pituitary secretes: *oxytocin* and *antidiuretic hormone* (ADH, also called *vasopressin*).

- These (oxytosin and ADH) are actually synthesized in the hypothalamus and stored within the axon terminals in the posterior pituitary

Diseases of the anterior pituitary gland

1. Mass effect

- Masses that can affect the pituitary: adenomas or carcinomas
- Adenomas can be secretory or non secretory .
- pituitary carcinomas are rare and usually non-secretory

Mass effects of pituitary adenomas or cacinomas

Signs and symptoms :

*Radiographic abnormalities of sella turcica :sellar expansion, bony erosions.

*Compression of the optic chiasm (the X-shaped structure formed at the point below the brain where the two optic nerves cross over each other) resulting in visual field abnormalities. (see next slide)

*Elevated intracranial pressure: headache, nausea, vomiting. Note: any mass in the cranium (inside the skull) can cause increased intracranial pressure

*seizures.

*Cranial nerve palsies.

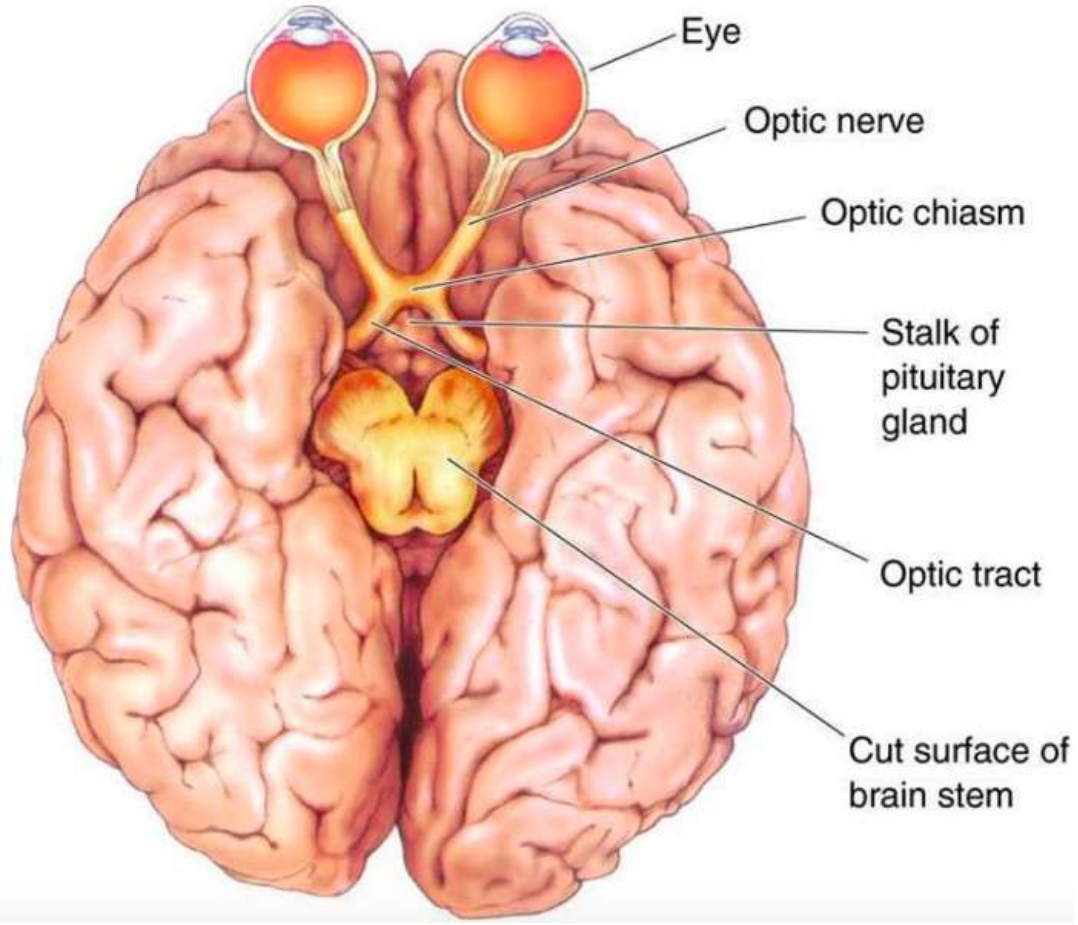
*pituitary apoplexy.. More details in a minute!

The optic chiasm is the X shaped structure formed by cross-over of the optic nerves.

The pituitary is very close to this chiasm

So: a mass in the pituitary can compress the chiasm.. This will affect vision.

Note: because of this cross over, the right optic nerve supplies the left eye and vice versa.. So a defect in the right optic nerve will cause visual field defect in the left eye (the contralateral eye)



Pituitary apoplexy=السكتة النخامية

- Acute hemorrhage into an adenoma, which causes rapid enlargement of the lesion. This will result in decreased consciousness.
- This is a neurosurgical emergency…. Can cause sudden death.
- The word apoplexy means anger or rage.
- Apoplexy in medicine: is bleeding within internal organ.. Example: ovarian apoplexy, pituitary apoplexy.

Pituitary adenomas

- Functional or nonfunctional.
- Functional: usually **one cell type** and one hormone produced.
- Classified according to the hormones they produce.

Types of pituitary adenomas

- Prolactinomas.. 20-30%.. The most common
- Null cell adenoma… 20%.. Non secretory
- ACTH cell adenoma.. 10-15%
- Gonadotroph cell adenoma… 10-15%
- GH cell adenoma… 5%
- Mixed GH/Prolactn adenoma.. 5%
- TSH cell adenoma… 1%.. Least common
- pleurihormonal… 15%
- *AS USUAL: DON'T MEMORISE THE NUMBERS!. The most common one is important and the fact that TSH adenomas are the rarest is also important.*

Pituitary adenomas

- In clinical practice 10% of intracranial neoplasms are pituitary adenomas.
- But pituitary adenomas can be an incidental finding in 25% of autopsies.
- Peak.. 4^{th} to 6^{th} decades.
- Mostly **single** lesions= solitary
- Can be divided into micro and macro adenomas according to size.. Cutoff point: 1cm.

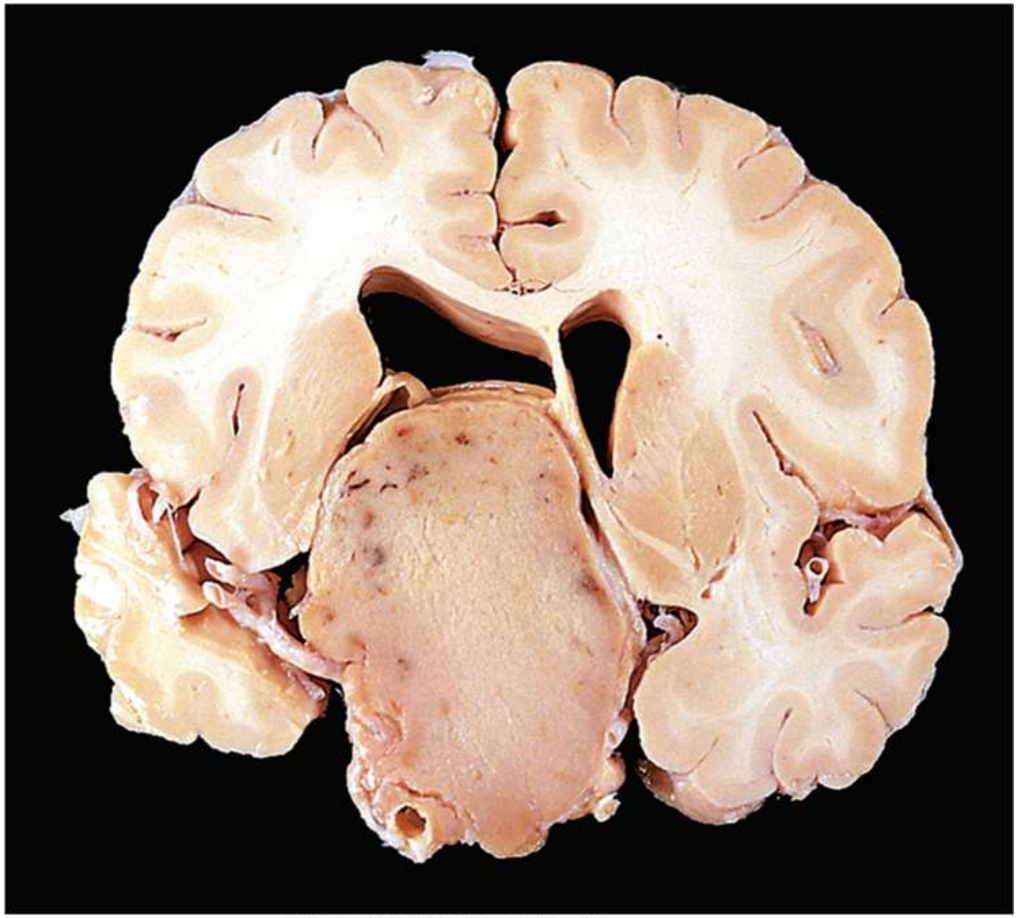
Macroscopic appearance

Gross features of adenomas

- The usual adenoma is a **well-circumscribed**, lesion that if small, is confined by the sella turcica

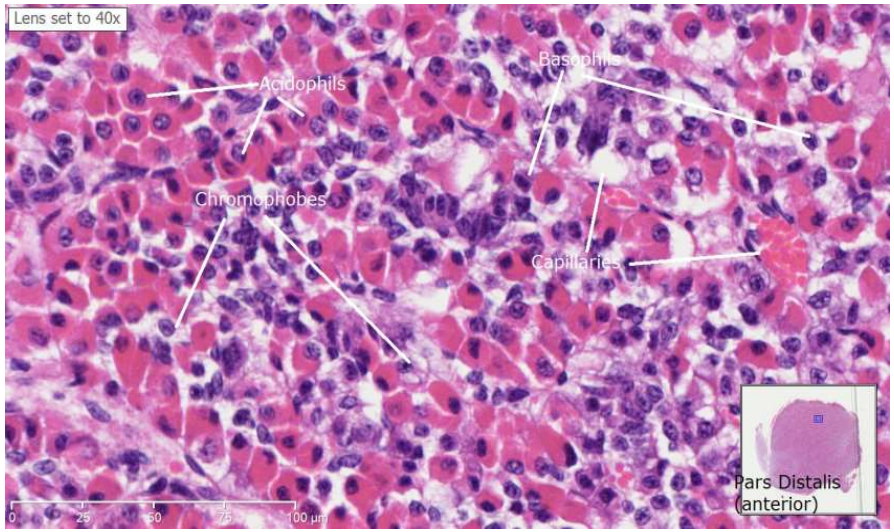
- In 30% of cases, the adenomas are non-encapsulated and infiltrate adjacent bone, dura and brain.

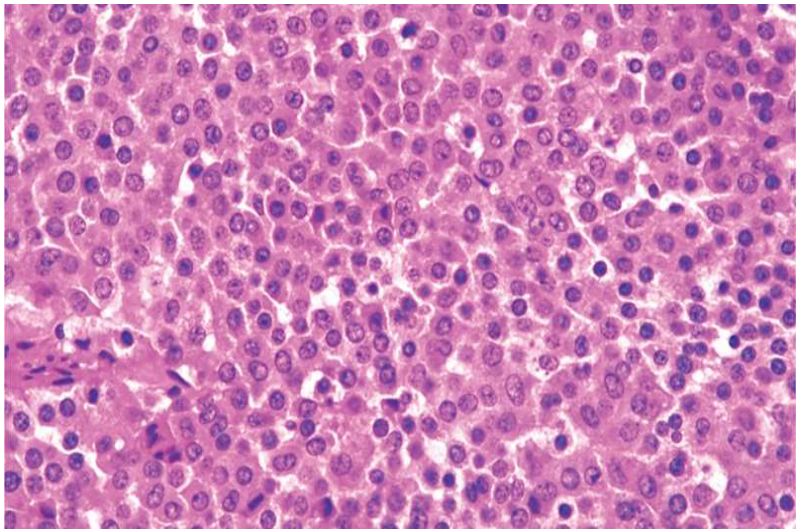
Pituitary adenoma



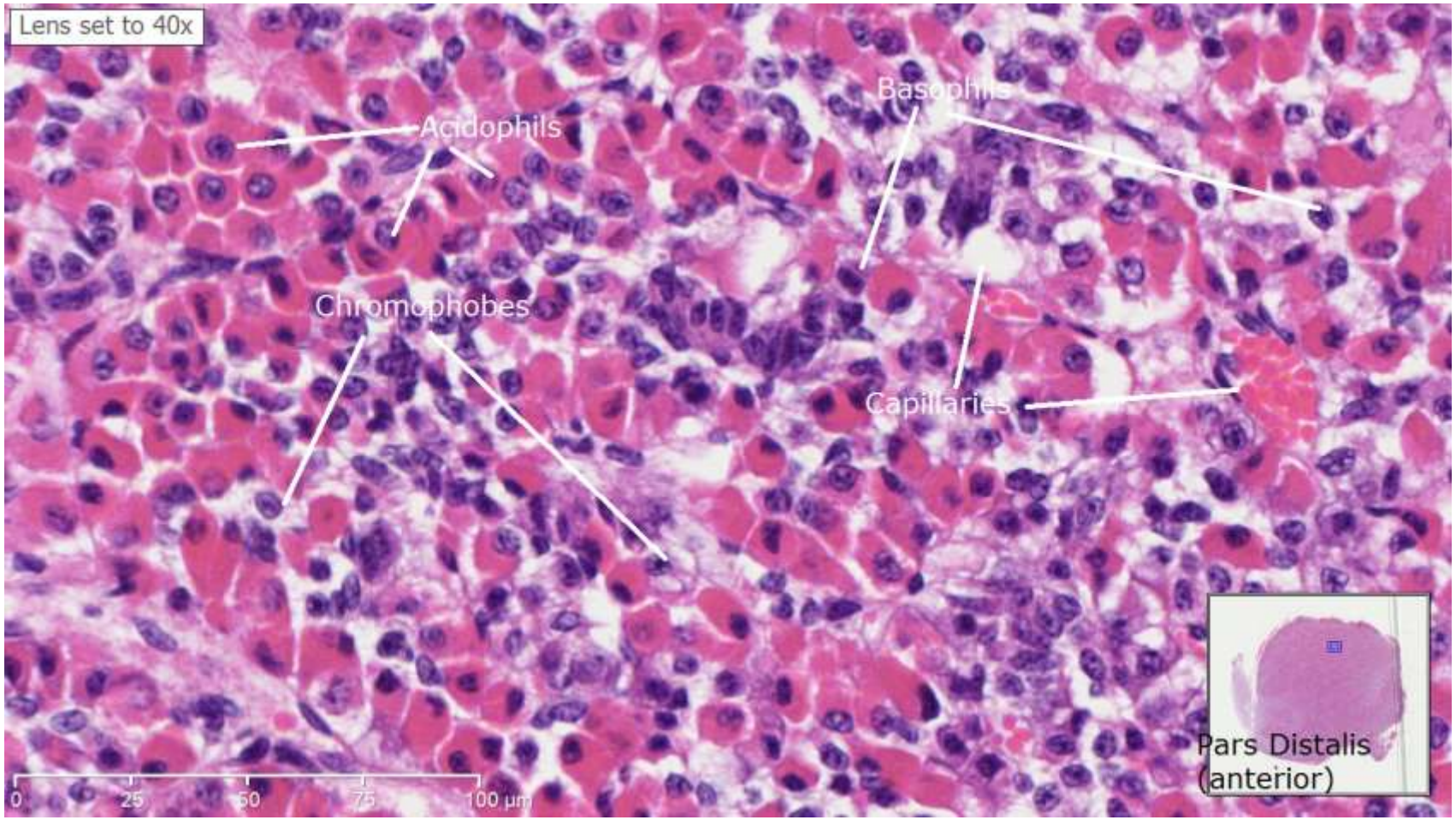
Pituitary adenoma

- Monomophic: one cell type.. All cells look similar, whereas in the normal pituitary several cell types exist.
- Can you see the difference between these two pics?

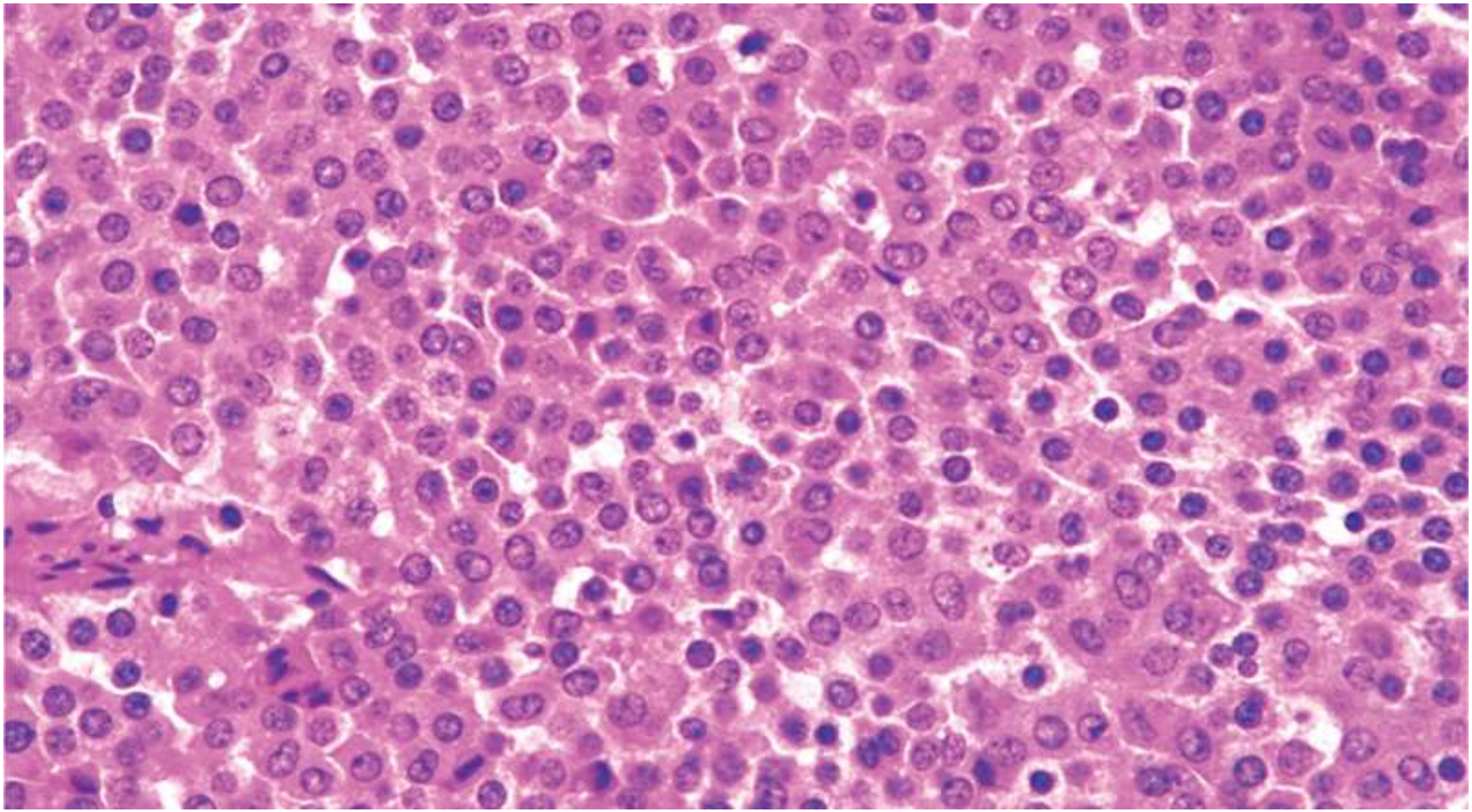




Normal pituitary.. Several cell types



Adenoma.. One cell type = monomorphic appearance



- *prolactinomas*

These are adenomas that produce prolactin.= hyperprolactinemia

Hyperprolactinemia causes:

a. Amenorrhea
b. galactorrhea,
c. infertility

Growth Hormone-Producing (Somatotroph) Adenomas

Increased growth hormone can cause Gigantism or acromegaly*:*

If a growth hormone-secreting adenoma occurs before the epiphyses closes (in children) it causes *gigantism.*

- gigantism: generalized increase in body size, with disproportionately long arms and legs.

gigantism

acromegaly

If elevated levels of growth hormone persist, or develop after closure of the epiphyses, affected persons develop *acromegaly,* in which:

1. Growth is most conspicuous in soft tissues, skin, and viscera and in the bones of the face, hands, and feet
2. Enlargement of the jaw results in its protrusion with separation of the teeth.
3. Enlarged hands and feet with broad, sausage-like fingers

acromegaly

- acromegaly

Corticotroph cell adenomas

- **may be:**

May cause *hypercortisolism= increased cortisol , m*anifested clinically as ***Cushing syndrome***

Gonadotroph LH]-producing and FSH adenomas

- Can be difficult to recognize, because they secrete hormones inefficiently, and the secretory products usually do not cause a recognizable clinical syndrome.

Pituitary carcinomas

- *are exceedingly rare and i*n addition to local extension beyond the sella turcica, these tumors virtually always demonstrate **distant metastases.**

- **As a general rule: Most endocrine carcinomas are diagnosed depending on behavior (presence of metastases) and not on histological appearance. i:e under the microscope adenoma and carcinoma can look similar.. You need to know the clinical information and check if the patient has metastatic disease in order to call the lesion metastatic.**

Hypopituitarism:

Occurs if there is **Loss of at least 75% of anterior pituitary**

Causes:

a. *Congenital* absence(exceedingly rare)

b. Hypothalamic tumors, associated with posterior pituitary dysfunction.

C . Nonfunctioning pituitary adenomas .. Most common/ this occurs when the adenoma compresses normal pituitary tissue and affects its function.

d. Ischemic necrosis of the anterior pituitary, **Sheehan syndrome**(see next slide) e;g

e. Ablation of the pituitary by surgery or irradiation

f. Inflammatory lesions such as sarcoidosis or tuberculosis

g. Trauma and Metastatic neoplasms involving the pituitary.

Sheehan syndrome, or postpartum necrosis of anterior pituitary, is the most common form of clinically significant ischemic necrosis of the anterior pituitary.

- During pregnancy, the anterior pituitary enlarges considerably, because of an increase in the size and number of prolactin-secreting cells and this physiologic enlargement is not accompanied by an increase in blood supply
- The enlarged gland is thus vulnerable to ischemic injury, especially in women who experience significant hemorrhage and hypotension during the postpartum period

POSTERIOR PITUITARY SYNDROMES.

- Impairment of oxytocin synthesis and release has not been associated with significant clinical abnormalities.

- The clinically important posterior pituitary syndromes involve ADH= vasopressin

ADH deficiency

Causes *diabetes insipidus (DI)* characterized by excessive urination (polyuria) caused by an inability of the kidney to properly resorb water from the urine

SO: patients are thirsty and have polydipsia= excessive drinking

Diabetes insipidus can result from several causes,

a. Head trauma,
b. Neoplasms,
c. Inflammatory disorders
d. surgical procedures of the hypothalamus and pituitary,
e. idiopathic.

- The clinical manifestations of DI include:

a. The excretion of large volumes of **dilute** urine with an inappropriately **low specific gravity**

b. **Serum sodium and osmolality are increased as a result of excessive renal loss of free water resulting in thirst and polydipsia**

- Patients who can drink water generally can compensate for urinary losses; patients who are bedridden, or are limited in their ability to obtain water may develop life threatening dehydration.

Increased ADH= Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

In *(SIADH)* ADH excess is caused by several extracranial and intracranial disorders.

- This condition leads to **resorption of excessive amounts of free water, with resultant hyponatremia**.
- The most common causes of SIADH include;

a. The secretion of **ectopic** ADH by malignant neoplasms

b. Non-neoplastic diseases of the lung

c. local injury to the hypothalamus or neurohypophysis.

- The clinical manifestations of SIADH are dominated by hyponatremia, cerebral edema, and resultant neurologic dysfunction.

CHECK YOUR UNDERSTANDING

- A 31-year-old woman, who has two healthy children, notes that she has had **no menstrual periods** for the past 6 months, but she is not pregnant and takes no medications. Within the past week, she has noted **some milk production** from her breasts. She has been bothered by **headaches** for the past 3 months. After nearly hitting a bus while changing lanes driving her vehicle, she is concerned with **her vision**. Which of the following laboratory test findings is most likely to be present in this woman?
- A Increased serum cortisol
- B Lack of growth hormone suppression
- C Increased serum alkaline phosphatase
- D Hyperprolactinemia
- E Decreased serum TSH

Explanation of the case in the question.

- This patient has amenorrhea and galactorrhea.. These are manifestations of increased prolactin.
- Her vision is affected because of the mass effect of the prolactinoma.
- The headache is caused by the increased intracranial pressure caused by the mass (any increase in the components of the brain: brain tissue, fluid, blood or CSF will result in increased intracranial pressure).. Headache is one of the manifestations of increased intracranial pressure.

CHECK YOUR UNDERSTANDING/ Q2

- A 33-year-old previously healthy man has lateral **visual field deficits,** but his residual vision is 20/20. **His facial features have changed** over the past year. His **shoe size has increased**. A head CT scan reveals **enlargement of the sella turcica**. Which of the following hormones is most likely being secreted in excessive amounts in this man?
- A Antidiuretic hormone
- B Prolactin
- C ACTH
- D Growth hormone
- E Luteinizing hormone


THANK YOU!